IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

1. (withdrawn/currently amended) A process for the preparation of a depolymerized-LMW-epiK5-N,O-sulfate containing 40%-60% iduronic units and having a sulfation degree of from 2.3 to 2.9, which comprises

(a) treating a tertiary or quaternary organic base salt of a depolymerized-LMW-epiK5-N-sulfate containing 40%-60% iduronic units with a sulfation agent under O-oversulfation conditions to obtain a depolymerized-LMW-epiK5-amine-O-oversulfate;

(b) submitting the depolymerized-LMW-epiK5-amine-O-oversulfate thus obtained to a selective O-desulfation to obtain a depolymerized-LMW-epiK5-amine-O-sulfate;

(c) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-amine-O-sulfate thus obtained with a O-sulfation agent to obtain a depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate; and

(d) submitting the depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate thus obtained to a N-sulfation reaction and isolating the depolymerized-LMW-epiK5-N,O-sulfate thus obtained.

2. (withdrawn/currently amended) The process ~~Process~~ according to claim 1, wherein the depolymerized-LMW-epiK5-N,O-sulfate thus obtained is isolated as the sodium salt thereof which is optionally converted into another pharmaceutically acceptable salt thereof.

3. (withdrawn/currently amended) The process ~~Process~~ according to claim 2, wherein said other salt is that with another alkaline metal, an alkaline-earth metal, aluminum or zinc.

4. (withdrawn/currently amended) The process ~~Process~~ according to claim 1, wherein the starting depolymerized-LMW-epiK5-N-sulfate is obtained by submitting a K5-N-sulfate, in any order,

(i) to C5-epimerization with a D-glucuronyl C5-epimerase isolated, purified and either in solution or immobilized on a solid support, at a pH of approximately 7, at a temperature of approximately 30°C and for a time period of 12-24 hours in the presence of at least one bivalent ion selected among calcium, magnesium, barium and manganese; and

(ii) to a nitrous depolymerization followed by reduction, normally with sodium borohydride.

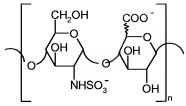
5. (withdrawn/currently amended) The process ~~Process~~ according to claim 4, wherein the starting depolymerized-LMW-epiK5-N-sulfate is obtained according to the sequence (i)-(ii) and has a mean molecular weight of from about 1,500 to about 12,000.

6. (withdrawn/currently amended) The process ~~Process~~ according to claim 5, wherein, said mean molecular weight is from about 1,500 to about 7,500.

7. (withdrawn/currently amended) The process ~~Process~~ according to claim 4, wherein the starting depolymerized-LMW-epiK5-N-sulfate is obtained according to the sequence (ii)-(i) and has a mean molecular weight of from about 4,000 to about 12,000.

8. (withdrawn/currently amended) The process ~~Process~~ according to claim 7, wherein said molecular weight is of from about 5,000 to about 7,500.

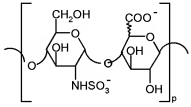
9. (withdrawn/currently amended) The process ~~Process~~ according to claim 1, wherein the starting depolymerized-LMW-epiK5-N-sulfate consists of a mixture of chains in which at least 90% of said chains has the formula I



(I)

in which 40%- 60% of the uronic units are those of iduronic acid, n is a integer from 2 to 20 and the corresponding cation is chemically or pharmaceutically acceptable.

10. (withdrawn/currently amended) The process ~~Process~~ according to claim 1, wherein said starting depolymerized-LMW-epiK5-N-sulfate consists of a mixture of chains in which the preponderant species has the formula I'a



(I'a)

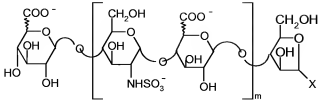
wherein 40% to 60% of the uronic units are those of iduronic acid and p is an integer from 4 to 8.

11. (withdrawn/currently amended) The process ~~Process~~ according to claim 1, wherein said starting depolymerized-LMW-epiK5-N-sulfate presents a 2,5-anhydromannitol unit of structure (a)

(a)

in which X represents a hydroxymethyl group, at the reducing end of the majority of the chains in said mixture of chains.

12. (withdrawn/currently amended) The process ~~Process~~ according to claim 9, wherein said starting depolymerized-LMW-epiK5-N-sulfate consists of a mixture of chains in which the preponderant species has the formula I'b



(I"b)

in which X hydroxymethyl, m is 4, 5 or 6, the corresponding cation is a chemically or pharmaceutically acceptable ion and the glucuronic and iduronic units are present alternately, the non reducing extremity being a glucuronic or iduronic unit, with a ratio glucuronic/iduronic from 45/55 to 55/45.

13. (withdrawn/currently amended) A process for the preparation of depolymerized-LMW-K5-N,O-sulfates having a sulfation degree of from 2.3 to 2.9 and of their pharmaceutically acceptable salts, which comprises

(ii) submitting a K5-N-sulfate to a nitrous depolymerization to obtain a depolymerized-LMW-K5-N-sulfate having a mean molecular weight higher than 4,000;

(i) submitting the depolymerized-LMW-K5-N-sulfate thus obtained to a C5-epimerization with D-glucuronyl-C5-epimerase to obtain a depolymerized-epiK5-N-sulfate containing from 40% to 60% iduronic units;

(a) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-N-sulfate thus obtained with a sulfation agent under the conditions of O-oversulfation to obtain a depolymerized-LMW-epiK5-amine-O-oversulfate;

(b) submitting the depolymerized-LMW-epiK5-amine-O-oversulfate thus obtained to a selective O-desulfation to obtain a depolymerized-LMW-epiK5-amine-O-sulfate;

(c) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-amine-O-sulfate thus obtained with a O-sulfation agent to obtain a depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate; and

(d) submitting the depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate thus obtained to a N-sulfation reaction and isolating the

depolymerized-LMW-epiK5-N,O-sulfate thus obtained as the sodium salt thereof which is optionally converted into another pharmaceutically acceptable salt.

14. (withdrawn/currently amended) The process ~~Process~~ according to claim 13, wherein at the end of step (ii) a depolymerized-LMW-K5-N- sulfate having a mean molecular weight of from about 5,000 to about 7,500 is obtained.

15. (withdrawn/currently amended) The process ~~Process~~ according to claim 13, wherein at the end of step (ii) a depolymerized-LMW-K5-N- sulfate having a mean molecular weight of from about 6,000 to about 7,500 is obtained.

16. (withdrawn/currently amended) A process for the preparation of depolymerized-LMW-K5-N,O-sulfates having a sulfation degree of from 2.3 to 2.9 and of their pharmaceutically acceptable salts, which comprises

(i) submitting a K5-N-sulfate to a C5-epimerization with a D-glucuronyl C5-epimerase isolated, purified and in solution or immobilized on a solid support, at a pH of about 7, at a temperature of about 30°C and for a period of time of 12-24 ore in the presence of at least one bivalent ion selected among calcium, magnesium, barium and manganese;

(ii) submitting the epiK5-N-sulfate thus obtained to a nitrous depolymerization followed by a reduction, normally with sodium borohydride, to obtain a depolymerized-LMW-K5-N-sulfate;

(a) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-N-sulfate thus obtained with a sulfation agent under O-oversulfation conditions to obtain a depolymerized-LMW-epiK5-amine-O-oversulfate;

(b) submitting the depolymerized-LMW-epiK5-amine-O-oversulfate thus obtained to a selective O-desulfation to obtain a depolymerized-LMW-epiK5-amine-O-sulfate;

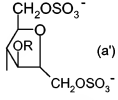
(c) treating a tertiary or quaternary organic base salt of the depolymerized-LMW-epiK5-amine-O-sulfate thus obtained with an O-sulfation agent to obtain a

depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate; and

(d) submitting the depolymerized-LMW-epiK5-amine-O-sulfate containing at least 80% 6-O-sulfate thus obtained to a N-sulfation reaction and isolating the depolymerized-LMW-epiK5-N,O-sulfate thus obtained as the sodium salt thereof which is optionally converted into another pharmaceutically acceptable salt.

17. (previously presented) A depolymerized-LMW-epiK5-N,O-sulfate obtainable according to claim 1.

18. (original) A depolymerized-LMW-epiK5-N,O-sulfate having a sulfation degree of from 2.3 to 2.9, a mean molecular weight of from about 1,500 to about 12,000 and, at the reducing end of the majority of its chains, the structure (a')



(a')

in which R represents hydrogen or SO_3^-, or a pharmaceutically acceptable salt thereof.

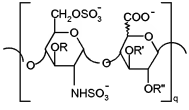
19. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 18, having a mean molecular weight of from about 1,500 to about 8,000 and a sulfation degree from 2.5 to 2.9.

20. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 19, having a sulfation degree of from 2.7 to 2.9.

21. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 20, having a mean molecular weight of about 6,000.

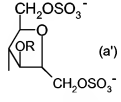
22. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 18, having a mean molecular weight of about 6,000, a sulfation degree of from 2.7 to 2.9, a content of 80%-95% in glucosamine 6-O-sulfate, of 95%-100% in glucosamine N-sulfate, of 45%-55% in glucosamine 3-O-sulfate, of 35%-45% in glucuronic acid 3-O-sulfate, of 15%-25% in iduronic acid 2-O-sulfate and presenting an unity (a') at the reducing end of the majority of its chains, or a pharmaceutically acceptable salt thereof.

23. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 18 consisting of a mixture of chains in which at least 80% of said chains has the formula III



(III)

wherein the 40%-60% of the uronic units are those of iduronic acid, q is an integer from 2 to 17, R, R' and R'' are hydrogen or SO_3^- for a sulfation degree of from 2.3 to 2.9, and the reducing end of the majority of the chains in said mixture of chains presents a sulfated 2,5-anidromannitol unit of structure (a')



(a')

in which R represents hydrogen or SO_3^- and the corresponding cation is chemically or pharmaceutically acceptable.

24. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 23, consisting of a mixture of chains in which at least 80% of said chains has the formula III wherein q is an integer from 2 to 14.

25. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 23, consisting of a mixture of chains in which at least 80% of said chains has the formula III wherein q is an integer from 2 to 11.

26. (currently amended) The [[A]] depolymerized-LMW-epiK5-N,O-sulfate according to claim 23, consisting of a mixture of chains in which the preponderant species is a compound of formula III wherein q is 8 or 9, R is 45%-55% SO_3^-, R' is 35%-45% SO_3^- in glucuronic acid, R" is 15%-25% SO_3^- in iduronic acid, for a sulfation degree of from 2.7 to 2.9.

27. (currently amended) A pharmaceutical ~~Pharmaceutical~~ composition comprising, as an active ingredient, a pharmacologically active amount of a depolymerized-LMW-epiK5-N,O-sulfate according to claim 17, or of a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutical carrier.

28. (withdrawn) A method for the regulation of the coagulation in a mammal, which comprises administering to said mammal in need of said regulation of the coagulation an effective amount of a depolymerized-LMW-epiK5-N,O-sulfate according to claim 17 or of a pharmaceutically acceptable salt thereof.

29. (withdrawn) A method for preventing or treating thrombosis in a mammal, which comprises administering to said mammal an effective amount of a depolymerized-LMW-epiK5-N,O-sulfate according to claim 17 or of a pharmaceutically acceptable salt thereof.

30. (withdrawn) The method of claim 28, wherein said effective amount is administered in a pharmaceutical composition comprising from 5 to 100 mg of said depolymerized-LMW-epiK5-N,O-sulfate or of a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutical carrier.

31. (withdrawn) The method of claim 29, wherein said effective amount is administered in a pharmaceutical composition comprising from 5 to 100 mg of said depolymerized-LMW-epiK5-N,O-sulfate or of a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutical carrier.

32. (original) A pharmaceutical composition comprising, as active ingredient, a pharmacological active amount of an (epi)K5-amine-O-oversulfate-derivative having a sulfation degree of from 2 to 4, or of a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutical carrier.

33. (original) The composition of claim 32, wherein said (epi)K5-amine-O-oversulfate-derivative is obtainable by treating a tertiary or quaternary organic base salt of an (epi)K5-N-sulfate-derivative with a O-sulfating agent under O-oversulfation conditions.

34. (original) The composition of claim 32, wherein said (epi)K5-amine-O-oversulfate-derivative is obtainable by treating a tertiary or quaternary organic base salt of an (epi)K5-N-sulfate-derivative with a O-sulfating agent under O-oversulfation conditions, said salt with said organic base having been isolated immediately after its formation, at a pH of from about 5 to about 9.

35. (original) The composition of claim 32, wherein said (epi)K5-amine-O-oversulfate-derivative is obtainable by

(a1') treating an (epi)K5-N-sulfate-derivative, in its acidic form, with a tertiary or quaternary organic base and isolating its salt with said tertiary or quaternary organic base immediately after its formation, at a pH of from about 5 to about 9;

(a2') treating said tertiary or quaternary organic base salt of said (epi)K5-N-sulfate-derivative with an O-sulfation agent under the conditions of an O-oversulfation and isolating the (epi)K5-amine-O-oversulfate-derivative as the sodium salt thereof which can subsequently be converted into another salt.